NIH Center for Scientific Review

peer review notes

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CSR's Director Goes to Capitol Hill

"It was remarkable," said CSR Director Dr. Richard Nakamura, "to be invited to explain the value of NIH peer-reviewed science to both House and Senate staffers." Though NIH officials cannot lobby Congress, Dr. Nakamura took the opportunities to tell it like it is.

"Foreign officials have beaten a path to CSR," he said. "Officials from China, S. Korea, Japan, India and many countries continue to come to CSR because they want to copy the winning formula NIH uses to identify and fund the most promising grant applications: Peer Review."

How Peer Reviewed Research Has Advanced U.S. Health and Wealth

After explaining how scientific experts from academia and industry review NIH grant applications, he focused on how peer-reviewed research has helped advance U.S. health and wealth:

- 1.35 million deaths are prevented each year due to NIH research advances
- 70% of major drugs were developed or made possible by NIH-funded research

- **Research-related gains in average life expectancy from 1970 to 2000 have an economic value estimated at $95 trillion post-1970, or about $3.2 trillion per year**

Will the Future Be as Bright as the Past?

Dr. Nakamura presented a sobering answer to this question: While NIH appreciates the support Congress has it given during difficult times, it's important to know that success rates for NIH grants are at an historic low, and the percentage of U.S. GDP invested in research has gone down, while China, Brazil, S. Korea, India have increased their investments.

"We should realize we have reached our Sputnik moment," said Dr. Nakamura. "China has doubled funding for medical research every five years for the last 30 years, and plans to overtake us in the next five years."

He concluded by saying, "NIH peer review might not be perfect, but it remains a proven way to help the U.S. make the public investments it needs to empower researchers across the country to advance U.S. science, health and economic growth."

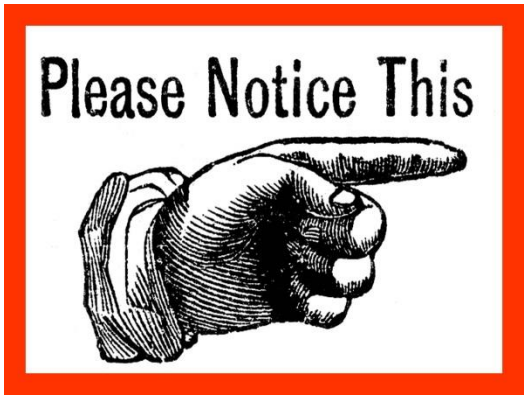
View his poster presentation as well as his PowerPoint slides, which you may use without seeking permission.

Special Thanks to the Congressional Event Organizers

- ***The Coalition for the Advancement of Health Through Behavioral and Social Science Research*** organizing an exhibition for the U.S. House June 24, 2015, to celebrate the 20th anniversary of the NIH Office of Behavioral and Social Sciences Research.

- ***The Coalition to Promote Research*** organized the U.S. Senate briefing on September 22, 2015: NIH Priority Setting: How Peer Review Assists the NIH in Selecting the Best Science.

Good to Know: NIH and Peer Review News



- **Reviewers' Personal Data Was Not Affected by the Recent Hack of the Office Personnel Management —** OPM website.

- **What Are Your Chances of Getting NIH Funding? —** Rock Talk article.

- **NIH Regional Seminars on Program Funding and Grants Administration:** October 14-16, 2015, in San Diego, CA — more.

- **Application/Review Policy Changes Coming So Stay Tuned**:
  - Changes to Enhance the Reproducibility of NIH Research
  - Changes related to balancing sex in cell and animal studies.

- **New Plan for Building a Large Cohort to Advance the Precision Medicine Initiative** — more.

Help Applicants at Your Institution by Using New CSR Outreach Resources

Reviewers have great insights into the NIH peer review process. To help you share them with applicants at your institution, we pulled together outreach resources you can use: slides, handouts and videos.

New Outreach Slides

We just created a set of PowerPoint slides you can use to develop your own outreach presentations. We added helpful details in the note sections of many slides. You can download them from our Outreach Slides Web page.

You may use these slides without seeking permission.

We Only Ask that You . . .

- ***Check for updates as policies and practices can change***

- ***Do not imply that your presentation is an official NIH/CSR presentation***

- ***Contact us if you have questions about the slides:*** CSRCOMMUNICATIONSOFFICE@csr.nih.gov

Handouts You Can Print and Use

- ***Insider's Guide to Peer Review for Applicants***

- ***NIH Grant Application Submission and Review Useful Web Links***

- ***What Happens to Your Grant Application: A Primer for New Applicants***

- ***Jumpstart Your Career by Becoming an Early Career Reviewer***

These handouts are official CSR publications and cannot be changed. However, you can create customized handouts with any of the information in them so long as you don't imply they are NIH/CSR publications.

Videos

CSR's peer review videos are often featured in seminars to help applicants better understand NIH peer review:

- ***NIH Peer Review Revealed***

- ***Jumpstart Your Research Career with CSR's Early Career Reviewer Program***

- ***NIH Tips for Applicants***

You can download QuickTime files from our video page so you don't have to worry about possible problems in streaming videos to a live audience.

Our archived webinar videos can also be useful if you want to give more detailed information. We have archived webinars for R01, R15, fellowship and small business applicants.

New Webinars for Applicants and University Grants Administrators

Pass the word to applicants, mentors and research administrators at your institution: the NIH Center for Scientific Review will host two "Meet the Experts in NIH Peer Review" webinars in early November 2015. The goal is to give useful insights into the application submission and review processes.

Each Webinar Will Have a Different Focus

Webinar Focus	Date
University Research Administrators	November 5, 2015
Research Project Grants (R01)	November 6, 2015

Both webinars will run from 2:00 to 4:00 p.m. EST, including a 30 minute Q&A period.

Viewers Will See Presentations by Five CSR/NIH Experts

- The Review of Your NIH Grant Application Begins Here
- What You Need to Know about Application Receipt and Referral
- How Your Application Is Reviewed
- Key Things to Know About the NIH Grants Program
- Jumpstart Your Career with CSR's Early Career Reviewer Program (applicant webinar only)

How to Participate in the Webinar

- ***Go to www.csr.nih.gov/webinar to register for the webinar you wish to join by Monday, October 29.*** You will not need to download special software. You will just need a reliable Internet connection and browser.

- ***Submit questions for the Q&A session before or during the webinar*** by sending them to the moderator at AskExperts@csr.nih.gov.

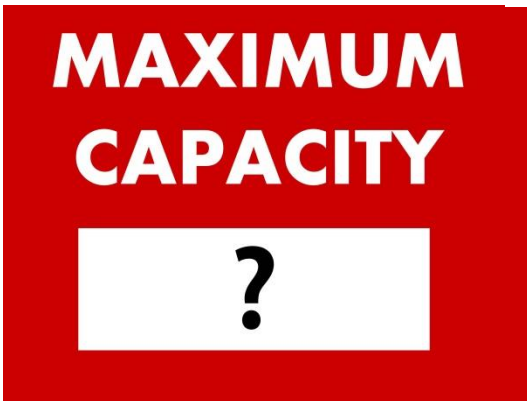
- ***Go to www.csr.nih.gov/webinar on the day/time your webinar is scheduled.*** Click on the link that will be provided there to view it.

View Archived Webinars

- ***View archived webinars now:*** Our webinar webpage has links to webinars for R01, R15, Small Business and Fellowship grant applicants.

- ***View our 2015 Webinars and PowerPoints about a month after broadcast*** on our webinar webpage.

Understanding the Capacity of NIH's Peer Review System



"There . . . are concerns that NIH's demand for peer reviewers may have exceeded the capacity of our current grantees to support it," said Dr. Sally Rockey, the former Director of the NIH Office of Extramural Research. "Therefore, over the past two years my office has been evaluating the level of service that most peer reviewers are willing and able to provide, and how peer review service fits within the scope of reviewers' other professional responsibilities."

OER's study found that there is a deep level of commitment to NIH peer review in the community. Based on what reviewers said about their preferred review loads, extra capacity exists in the peer review system.

Key Results

- More than 80% of mid-career R01 recipients have served as reviewers at least once in the past five years.
- 88% of respondents who reported having been invited to review in the prior year had served at least once.
- ~51% of respondents reported that peer review of grants should comprise less than 5% of their professional effort, but another 46% reported that peer review of grants should make up 5-10% of their worktime.
- Respondents reported that they considered an assignment load of 6 applications per meeting, and 1 – 2 meetings per year, to be reasonable expectations. The typical load at CSR is more than this, and NIH would be hard pressed to review all the applications the scientific community submits if this preference became the norm.
- ~3,500 qualified reviewers/year have not yet served in the last five years.

If 80% of these qualified reviewers agreed to serve, NIH could handle about 5,500 more applications a year.

"NIH has not tapped the full capacity of the peer review system," concluded Dr. Rockey. "[However] much of our community gives their time and energy so that our peer review system stays strong. . . . We here at NIH want to underscore the importance of your participation in support of the scientific enterprise and thank you for making the NIH peer review system the gold standard for the world."

CSR Is Working to Engage Qualified Reviewers Who Haven't Served

As we reported in our May Peer Review Notes, our Scientific Review Officers are using lists of grantees who haven't served when they recruit reviewers. In addition, we have created a new way for researchers to volunteer to serve on our review groups. See our Become a Reviewer Web page.

Learn More and Join the Conversation on the Rock Talk Blog

The Power of Peer Review: New Treatment Targets "Persister" Cells in Chronic Infection

Tabloid headlines hyping lethal outbreaks of antibiotic-resistant, "flesh-eating" bacteria such as MRSA may be sensationalistic, but antibiotic resistance among common disease-causing bacteria is indeed an increasingly urgent medical problem.

Against a tide of such bad news, Dr. Kim Lewis, director of the Antimicrobial Discovery Center and University Distinguished Professor at Northeastern University, showed that a small, creative research team can still blaze trails to new treatments for infectious diseases.

The big surge in his research began in large part when he applied for an NIH Transformative Research Award. In creating the award, the NIH set out to fund high-risk, high-reward proposals with the potential to change conventional wisdom about fundamental biology. Dr. Lewis' creative thinking was recognized by his scientific peers, who reviewed his application. And they "believed he had the experience and expertise to follow through," said Dr. Christopher Taylor, Program Officer at the Respiratory Diseases Branch of the National Institute of Allergy and Infectious Diseases (NIAID).

The gamble has paid off: Dr. Lewis and his team have discovered at least one entirely new class of promising antibiotics, as well as new treatment strategies for attacking persistent bacterial infections.

Beyond Conventional Wisdom

The conventional wisdom is that antibiotic resistance arises because bacteria mutate, acquiring small genetic alterations at random. Sometimes a specific mutation alters function in a way that allows the mutant to survive antibiotic treatment, and to expand its numbers, while bacterial brethren lacking the key genetic change die. The rise of bacterial strains resistant to multiple antibiotics is associated with an accumulation of adaptive genetic alterations acquired over generations.

Infectious disease is often untreatable, even when caused by bacteria that are not resistant to antibiotics. As Dr. Lewis pondered this he thought about bacterial cells called "persisters." "The NIH asked grant applicants to transform a field of science, and we promised to transform our understanding of chronic disease by investigating the link between the persister cells and chronic disease," he said.

Persisters represent a small percentage of bacterial cells within an infectious population that becomes physiologically dormant. They evade destruction by treatments that kill energetically active cells. The dormant cells appear to become active again when treatment ends and reestablish infection. Persisters normally are genetically the same as non-dormant, vulnerable cells, but Dr. Lewis wanted to know if mutated persisters also existed and if they could further boost the likelihood of chronic infection.

For decades researchers have known that a bacterial gene called *hipA* triggers dormancy when it is activated. Dr. Lewis wanted to know if *hipA* existed in mutant forms in cells that acted as "super persisters" in chronic infection. Dr. Lewis and his research collaborators recently found that certain *hipA* mutants are indeed associated with tolerance to several antibiotics in chronic urinary tract infections caused by *E. coli*.

New Discoveries and Treatments

Dr. Lewis had other funding and projects, and he has been able to explore several other bacterial species to search for clues about persisters. Dr. Lewis and his colleagues found a way to culture previously unculturable bacteria. This feat allowed them to investigate previously uncultured species as an untapped source of potential new antibiotics. Dr. Lewis wanted to know if any of the newly discovered antibiotic-like molecules could kill bacteria responsible for human diseases and their persister cell populations. Many did.

The iChip Dr. Lewis and his team are using to culture in soil bacteria that were previously unculturable and to identify those that may produce new antibiotics. Photo: Slava Epstein/Northwestern University.

"We did not expect when we launched the project to find that so many molecules eradicate persisters, nor were we proposing a drug-discovery program at the time," Dr. Lewis said. One of the team's antibiotic discoveries, called teixobactin, made

headlines when the researchers published their findings in January 2015. It kills MRSA and other pathogens, acts differently than current antibiotics, and raises hope that resistance might not emerge for decades.

Dr. Lewis' research team has found that *Borrelia burgdorferi*, the bacterium responsible for Lyme disease, exists in a non-mutant persister form that can be coaxed out of dormancy and made vulnerable to reintroduction of antibiotic treatment through pulsed drug dosing. So far this strategy has been tested successfully in bacteria growing in lab cultures, but not yet in patients with chronic Lyme disease.

To translate discoveries into treatments, Dr. Lewis and his research collaborator Dr. Dallas Hughes, President of Novobiotic Pharmaceuticals, LLC recently received a Small Business Innovation Research (SBIR) grant through the NIAID to conduct preclinical development of teixobactin. As with all SBIR application, theirs was peer-reviewed by both industry and academic scientists.

"The reviewers appreciated not only that they found a new way to culture previously unculturable bacterial species, but also that the teixobactin molecule itself truly is novel," said Dr. Zuoyu Xu, Therapeutics Development Program Officer at the Bacteriology and Mycology Branch, NIAID. "They spoke with one voice and pushed this proposal to the top of the list." – *Jeff Norris*

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